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RECENT ADVANCES IN VIRUSES[1]

A BRIEF SURVEY OF RECENT WORK ON VIRUSES AND VIRUS DISEASES[2]

By Dr. EDWIN H. LENNETTE

SERVIÇO DE ESTUDOS E PESQUISAS SÔBRE A FEBRE AMARELA (YELLOW FEVER RESEARCH SERVICE)[3]

To formulate at the present time a concise, accurate and invariant definition of a virus is impossible due to the insufficiency of our knowledge concerning the nature of these disease incitants. Because the infectious agents classified as viruses possess the capacity to multiply or reproduce, because they showed marked specificity under natural conditions for certain hosts and tissues, are able to adapt themselves to new environmental conditions and to undergo variation, it is customary to regard them as living organisms. In the past viruses were characterized, and thus differentiated from bacteria, by the possession of a size at or below the limits of resolution possible with the usual microscopic methods, by their ability to pass through mineral or collodion filters which hold back bacteria, and by their total inability to reproduce in lifeless bacteriologic media. We now know, however, that invisibility and filtrability do not constitute valid criteria—some infectious agents possessing all the attributes of a virus and classed as such are visible and approximate the smallest bacteria in size while others pass with difficulty, or not at all, through filters which permit passage of the smallest bacteria. From the biologic standpoint the outstanding difference between viruses and bacteria appears to lie in the inability of viruses to propagate unless living cells are present; yet on closer analysis even this difference approximates the relative rather than the absolute in degree. Certain pathogenic bacteria, such as *Hemophilus influenzae* and *Pasteurella tularensis,* have become so highly parasitic that their nutritional requirements are

[1] Received for publication October 25, 1943.

[2] Presented on July 6, 1943, before the Seminario de Biologia, held in Rio de Janeiro from July 2 to 6, 1943, under the auspices of the University of Brazil.

[3] Maintained jointly by the Ministry of Education and Health of Brazil and the International Health Division of The Rockefeller Foundation.

met only by media containing animal tissues or tissue extracts, a condition which implies that certain enzyme systems vital to free-living forms are lacking. Viruses presumably possess even fewer enzyme systems, so few that only living cells can provide them with the conditions essential to multiplication.

The biologic position of the viruses is still uncertain, although a link to the recognized bacteria may perhaps exist through the rickettsiae, which some of the larger viruses resemble in certain respects, such as size, developmental cycles, tinctorial properties, etc.

THE NATURE OF VIRUSES

The numerous early attempts to gain insight into the nature and properties of the viruses were seriously hampered by the unavoidable use of crude extracts of infected tissues. Attempts at purification by chemical or physicochemical means were not lacking, but were attended with the loss of so much activity that the preparations were unsatisfactory for study.

The success of Stanley[4] in 1935 in isolating by chemical means from the juice of tobacco plants infected with tobacco-mosaic virus a crystalline protein possessing the properties of the virus gave new impetus to this field. While purely chemical methods on the whole have been found unsuitable for purification of viruses not endowed with the unusual stability of tobacco-mosaic virus, the development of the high-speed vacuum centrifuge has provided a valuable alternate method for purifying and concentrating virus preparations. Optical, ultracentrifugation, viscosity, diffusion, x-ray and other physical, as well as chemical, studies have been carried out on such purified preparations; the significance of some of the information obtained by correlating data from examinations by these methods is presented below.

It has been found possible to concentrate and purify the less stable viruses by repeated centrifugation in a high-speed air-driven vacuum centrifuge.[5,6] The procedure depends on the use of alternate cycles of low and high speed. Material thrown down at low speed (about 10,000 g) is discarded while sediments produced at high speed (*e.g.*, 50,000 g) are resuspended and subjected to another cycle of low- and high-speed centrifugation. The cycles are repeated until a homogeneous final preparation is achieved. The degree of homogeneity of the suspension as well as the particle size of the suspended material is checked in an analytical ultracentrifuge.[5,6]

The end-product obtained by repeated alternate high- and low-speed centrifugation is a protein with which are associated all the properties of the virus. Ultracentrifugal analysis of such virus proteins indicates that they possess remarkable molecular homogeneity. Calculations of the molecular weights of the virus-proteins from their sedimentation constants show that these proteins are unusual in that they are composed of molecules much larger than those of any proteins previously described.[7] Thus, the tobacco-mosaic virus, one of the most intensively investigated, has a molecular weight of forty-three million, computed in accordance with the known asymmetry of the virus particles.[8] The viruses of rabbit papilloma[9] and of eastern equine encephalomyelitis,[10] whose particles are assumed to be spherical, have molecular weights in the neighborhood of twenty million. As pointed out by Stanley[7] the virus proteins have many of the properties of ordinary molecules, and because of their tremendous size he groups them with the macromolecules of the colloidal chemist.

The validity of the figures assigned for molecular weight or for particle shape, for example, has been checked, whenever feasible, by one or more additional methods, singly or in combinations. The plant viruses have been the most intensively studied and tobacco mosaic virus protein is chosen here as an illustrative example; the data presented are taken from a recent review by Lauffer and Stanley.[8a] Tobacco-mosaic virus protein occurs in the liquid crystalline (mesomorphic or paracrystalline) state, and the crystals are held to be true crystals since they are double-refractive and on x-ray analysis give a typical crystalline pattern. This ability to exist in a liquid crystalline state implies that the molecules have a rodlike structure, an implication supported by the findings that the virus protein shows double refraction of flow, positive electrical birefringence and the Ganz depolarization effect. If the constants for sedimentation, specific viscosity, specific volume, diffusion and rotational diffusion for a virus protein, are known it is possible by use of the appropriate equations and various combinations of these constants to ascertain the size, shape and weight of the virus molecule. By such means the tobacco-mosaic virus protein has been calculated, as mentioned above, to have a molecular weight of forty-three million and to consist of asymmetric particles approximately 280 mμ × 15 mμ.[8b] X-ray diffraction data also indicate that the particles have a diameter of 15.2 mμ and a length greater than 120 mμ.

[4] W. M. Stanley, SCIENCE, 81: 644–645, 1935.
[5] T. Svedberg and K. O. Pedersen, "The Ultracentrifuge." Clarendon Press, Oxford, England, 478 pp., 1940.
[6] E. G. Pickels, *Chem. Reviews*, 30: 341–345, 1942.
[7] W. M. Stanley, *Jour. Phys. Chem.*, 42: 55–70, 1938.
[8] a. M. A. Lauffer and W. M. Stanley, *Chem. Reviews*, 24: 303–321, 1939. b. W. M. Stanley and C. A. Knight, *Cold Spring Harbor Symposia on Quantitative Biology*, 9: 255–262, 1941.
[9] J. W. Beard and R. W. G. Wyckoff, SCIENCE, 85: 201–202, 1937.
[10] A. R. Taylor, D. G. Sharp, Dorothy Beard and J. W. Beard, *Jour. Infect. Dis.*, 72: 31–41, 1943.

With the exception of vaccine virus, which is relatively quite stable, as well as being one of the largest known viruses, the animal viruses have enjoyed but little attention compared to the plant viruses. The large particle size of vaccine virus makes feasible its purification and concentration by comparatively simple centrifugational procedures, so that pure preparations of this virus have long been available for study. Infectivity of such preparations is attributed to the elementary bodies, which are sufficiently large to be examined under the ordinary microscope. Data derived from filtration of the virus through graded collodion membranes indicate that the virus has a particle size of 125 mμ to 175 mμ.[11] Barnard (according to Elford and Andrewes)[12] estimated the particle size, from photomicrographs taken with ultraviolet light, to be 160 mμ to 170 mμ. From the experimentally determined density and sedimentation constants and assuming an approximately spherical shape, Pickels and Smadel[13] calculated the average particle size of the elementary bodies to be 236 mμ to 252 mμ; direct measurements made by Green, Anderson and Smadel[14] from electron photomicrographs of elementary bodies are reported by Smadel and Hoagland[15] only to give values slightly lower than those obtained from ultracentrifugational analysis—no definite figures are given. However, since dehydration, an integral part of the technique of electron microscopy, is reported to decrease the diameter of elementary bodies approximately 14 per cent.,[16] a particle size somewhere around 200 mμ might be expected as compared with the particle size estimated from sedimentation experiments using hydrated elementary bodies.

In size, therefore, the elementary bodies of vaccine virus are close to the smallest bacteria. While pure plant viruses occur as liquid crystals, the elementary bodies of vaccinia morphologically resemble bacteria in structure. Electron microscope examination of the elementary bodies[14] reveals that they have a "bricklike" form within which can be seen five areas of condensation, darker than the surrounding ground substance. The nature of these condensed masses is unknown, as is true of similar masses found in many bacteria. The density of elementary bodies is 1.16,[16] greater than that of bacteria, 1.10[17] and less than that of protein, 1.33.[5] When treated with alkali, the elementary bodies swell and may burst, with resultant extrusion of the internal substance through the break in surface continuity.

None of the smaller animal viruses has been so intensively studied, from the physical standpoint, as vaccine virus, although there is now a perceptible trend to rectify this situation as evidenced by recent publications on rabbit papilloma,[18] mouse encephalomyelitis,[19] poliomyelitis,[20,21] equine encephalomyelitis[10] and influenza A[22] viruses. The latter virus will be used to illustrate how future work may serve to alter considerably our present conception of individual viruses.

The size of the infectious unit of influenza A virus in infectious mouse lung suspension has been estimated to be 80 mμ to 120 mμ by ultrafiltration[23] and 87 mμ to 99 mμ by centrifugation methods.[24] High-speed centrifugation of such suspensions results in sedimentation of more than 99 per cent. of the infectious material.[22,25] Electron micrographs show that the sedimented particles have a diameter of approximately 100 mμ,[22] which would be expected from the previous filtration and centrifugation studies. However, when infectious chick embryo allantoic fluid is spun in fields of centrifugal force capable of sedimenting mouse lung virus, infectivity remains about equally distributed between sediment and supernatant,[22] implying that the infectious unit in allantoic fluid actually is much smaller than in mouse lung suspensions. Since centrifugation of infectious and of normal mouse lung suspensions under identical conditions sediments particles of the same size, indistinguishable by electron microscopy or by chemical means,[22] it appears that the infectious unit is considerably smaller than the tissue particles on which it is adsorbed.[22] Bourdillon[26] has found that in infectious mouse lung suspensions only a small proportion of infectivity is associated with particles estimated from their diffusion constant to be about 6 mμ in diameter, while in allantoic fluid, which allows far less opportunity for adsorptive phenomena, up to one half of the infectivity is associated with particles of this size.

[11] W. J. Elford and C. H. Andrewes, *Brit. Jour. Exp. Path.*, 13: 36–42, 1932.
[12] W. J. Elford and C. H. Andrewes, *Brit. Jour. Exp. Path.*, 17: 422–430, 1936.
[13] E. G. Pickels and J. E. Smadel, *Jour. Exp. Med.*, 68: 583–606, 1938.
[14] R. H. Green, T. F. Anderson and J. E. Smadel, *Jour. Exp. Med.*, 75: 651–656, 1942.
[15] J. E. Smadel and C. L. Hoagland, *Bact. Rev.*, 6: 79–110, 1942.
[16] J. E. Smadel, E. G. Pickels and T. Shedlovsky, *Jour. Exp. Med.*, 68: 607–627, 1938.
[17] D. Ruffilli, *Biochem. Ztschr.*, 263: 63–74, 1933.
[18] W. R. Bryan and J. W. Beard, *Jour. Nat. Cancer Inst.*, 1: 607–673, 1941.
[19] S. Gard and K. O. Pedersen, SCIENCE, 94: 493–494, 1941.
[20] H. S. Loring and C. E. Schwerdt, *Jour. Exp. Med.*, 75: 395–406, 1942.
[21] E. Racker, SCIENCE, 96: 364–365, 1942.
[22] L. A. Chambers, W. Henle, M. A. Lauffer and T. F. Anderson, *Jour. Exp. Med.*, 77: 265–276, 1943.
[23] W. J. Elford, C. H. Andrewes and F. F. Tang, *Brit. Jour. Exp. Path.*, 17: 51–53, 1936.
[24] W. J. Elford and C. H. Andrewes, *Brit. Jour. Exp. Path.*, 17: 422–430, 1936.
[25] E. H. Lennette and F. L. Horsfall, *Jour. Exp. Med.*, 72: 233–246, 1940.
[26] J. Bourdillon, *Jour. Gen. Physiol.*, 25: 263–273, 1941.

Chambers *et al.*,[22] using infected allantoic fluid, obtained sedimentation constants which correspond to those of spherical particles 10–12.5 mμ in diameter; examination by electron microscopy of the sediments from ultracentrifugation showed a preponderance of spherical particles with a diameter of 11 mμ.

If these findings are substantiated, we must then consider influenza A virus to be one of the smallest known, and group it with the viruses of foot-and-mouth disease[27] and of poliomyelitis.[28,29] In addition, if its relatively low molecular weight, estimated at 650,000,[22] is confirmed, this would indicate that architectonically influenza A virus is closer to a virus such as tobacco-mosaic than to one like vaccinia or psittacosis, with molecular weights of $4{,}300 \times 10^{-6}$ and $8{,}500 \times 10^{-6}$ respectively.[8b]

The architectural similarity of poliomyelitis virus and of tobacco-mosaic virus perhaps is even closer, since Racker[21] has recently reported the isolation from infected mouse brains of liquid crystals which are protein in nature and which carry the infectivity of the virus.

Chemistry in the Virus

Attempts to study the composition of viruses have been, with few exceptions, restricted to elementary quantitative analyses because of the difficulty in obtaining more than minute amounts of purified material. However, important chemical differences among viruses can be shown only when the integral components, rather than the elements, of which they are built are known.

Of the twenty or so viruses which have been purified, all have been reported to contain nucleic acid. The nucleic acid present in plant virus proteins has invariably been of the ribo- or yeast-nucleic type, and hence the presence of the desoxy-ribose or thymo-nucleic type in the elementary bodies of vaccine virus[30] might be supposed to constitute a possible difference between viruses of plant and animal origin. Vaccine virus, however, appears to occupy, at least for the present, a unique position among the animal viruses, since the virus proteins of eastern equine encephalomyelitis[10] and of influenza A,[31] admittedly not as highly purified as elementary body suspensions, are reported to be of the yeast-nucleic type; the findings regarding chicken tumor I are contradictory.[32,33]

Tobacco-mosaic,[34] tobacco ring-spot[34] and rabbit papilloma[18] viruses appear to be composed entirely of nucleic and amino acids, since all the carbohydrate and phosphorus found can be accounted for on the basis of nucleic acid. Other plant viruses, as the latent mosaic virus,[34] may contain in addition a conjugated polysaccharide.

Lipoids have never been found associated with the plant viruses,[34] but the situation with the animal viruses is not clear—eastern equine encephalomyelitis virus appears to contain phospholipids, cholesterol and fatty acids;[10] vaccine virus contains phospholipids, cholesterol and neutral fat;[15] chicken tumor I contains a lipoid fraction of which about two thirds are probably a lecithin and the rest is unidentified,[32] while rabbit papilloma virus consists practically entirely of protein, having a fat content so small that its significance is questionable.[18]

The ability to obtain sufficient amounts of purified plant viruses has made feasible determinations of the amino acids composing the virus protein. Amino acids so far demonstrated in tobacco-mosaic virus protein include arginine, aspartic acid, cysteine, glutamic acid, leucine, lysine, phenylalanine, proline, serine, tryptophane and tyrosine;[35] alanine, histidine and glycine have not been demonstrated.[35] In addition, Stanley and Knight[8b] have been able to show that variations of tobacco-mosaic virus to produce a new strain as shown by serologic tests is also accompanied by specific changes in the amino acid content.

Antigenic Structure

The complexity in antigenic structure of a virus is reflected, within limits, by the number of distinct antibodies it is capable of producing.

The simplest viruses, antigenically, appear to be those of tobacco-mosaic[36] and of rabbit papilloma[37] since only one antibody responsible for both *in vitro* and *in vivo* immune phenomena has been detected. Most of the animal viruses studied thus far, however, give rise to at least two antibodies, one elicited by the virus proper and the other by the so-called soluble antigen, which is distinct and separable from the virus. The virus itself is presumed to give rise to the neutralizing antibodies, which when mixed with the virus *in vitro* render it noninfective. Soluble antigens, on the other hand, call forth antibodies which have no, or slight, neutralizing capacity, but react with the antigens *in vitro* to produce precipitation, agglutina-

[27] I. A. Galloway and W. J. Elford, *Brit. Jour. Exp. Path.*, 12: 407–425, 1931.

[28] Max Theiler and J. H. Bauer, *Jour. Exp. Med.*, 60: 767–772, 1934.

[29] W. J. Elford, I. A. Galloway and J. R. Perdrau, *Jour. Path. and Bact.*, 40: 135–141, 1935.

[30] C. L. Hoagland, G. I. Lavin, J. E. Smadel and T. M. Rivers, *Jour. Exp. Med.*, 72: 139–147, 1940.

[31] L. A. Chambers and W. Henle, *Jour. Exp. Med.*, 77: 251–264, 1943.

[32] A. Claude, SCIENCE, 87: 467–468, 1938.

[33] A. Claude, *Proc. Soc. Exp. Biol. and Med.*, 39: 398–403, 1938.

[34] W. M. Stanley, *Physiol. Rev.*, 19: 524–556, 1939.

[35] C. A. Knight and W. M. Stanley, *Jour. Biol. Chem.*, 141: 39–49, 1941.

[36] K. S. Chester, *Phytopathology*, 25: 702–714, 1935.

[37] J. G. Kidd, *Jour. Exp. Med.*, 68: 737–759, 1938.

tion or complement-fixation, depending upon the physical conditions present in the reacting system.

It appears likely, however, that as adequate techniques are devised additional antigens, complete or partial or both, will be discovered, since there is every reason to believe that the soluble antigen is not a single antigenic entity. Thus, the soluble antigen of infectious myxoma of rabbits has recently been found to contain two components designated A and B[38]—these are easily separable by physical methods, are heat-labile, probably protein in nature and are immunologically distinct. Vaccine virus is even more complex antigenically, since at least five antibodies appear in animals recovered from infection with this virus. Antibodies are produced against a heat-labile (L) and a heat-stable (S) antigen both of which are components of a single substance, LS,[39] shown by Smadel and Shedlovsky[40] to be an elongated protein molecule with a weight of 240,000 and an axis ratio in the neighborhood of 30:1. There is also present a nucleoprotein (NP) antigen[41] which gives rise to an antibody distinct from L and S antibodies, and like the L and S antigens, on injection into animals produces neither immunity to infection nor appreciable amounts of neutralizing antibody. The L, S and NP antigens are believed, according to recent findings, to be located on the surface of the infective unit, the elementary body.[15] Immune sera completely adsorbed with L, S and NP antigens to remove the corresponding antibodies still possess the ability to agglutinate elementary bodies and to neutralize the virus. The antigens responsible for the production of the X-agglutinins[38,41] and the neutralizing antibody are as yet little known, so that at present it is impossible to say whether they are distinct, related or identical.

Diagnosis

Much has been, and is being done, to develop simple, accurate and inexpensive methods to replace wholly or in part the slow, cumbersome and costly neutralization test, which has been the basic tool in diagnosis and in epidemiologic studies.

Through refinement of the antigens employed and determination of appropriate serum-inactivation temperatures, the specificity of the complement-fixation test has been brought to the stage where it is now possible to distinguish between experimental infections induced by the viruses of rabies, eastern and western equine encephalomyelitis, lymphocytic choriomeningitis, louping ill, St. Louis encephalitis and Japanese B encephalitis.[42] Preliminary experiences with the test in the diagnosis of human infections with some of these viruses are highly encouraging.[42,43]

With a few notable exceptions, attempts to demonstrate precipitation in specific animal virus antigen-antibody systems have been almost consistently negative. Recently, however, this field has been reopened with the finding that it is possible, at least in some cases, to demonstrate specific antigen-antibody union by the addition of an "indicator system" composed of bacteria[44] or of finely dispersed particles of collodion[45] whose aggregation leads to the formation of visible floccules.

Hirst[46] has observed that chick red cells are agglutinated in the presence of influenza virus and that agglutination can be prevented by immune serum. On the basis of these observations he has devised a method for titrating the agglutination-inhibiting substance in influenza immune sera[47,48] and has been able to show that it closely parallels the neutralizing antibody titer. The full implications of Hirst's findings are still unknown, but a similar technique has already been found applicable to vaccine virus infections.[49] The simplicity of the technique and the rapidity and ease with which a large number of sera can be examined have provided a valuable method for diagnosis and especially for epidemiologic investigations of those viral diseases to which it may be found applicable.

Epidemiology and Epizootiology

Within the last few years our conception of the epidemiology and pathogenesis of poliomyelitis has been considerably altered. This disease was generally believed to be spread solely, or almost so, by droplet infection, the virus gaining access to the central nervous system from the nasal mucous membrane by ascent along the olfactory nerve. Recent reinvestigation, in rather minute detail, of the pathogenesis and the pathology of poliomyelitis has brought forth considerable evidence that the alimentary tract is the usual portal of entry for the virus (reviewed in[50,51,52]).

[38] J. E. Smadel, S. M. Ward and T. M. Rivers, *Jour. Exp. Med.*, 72: 129–138, 1940.

[39] a. J. Craigie and F. O. Wishart, *Jour. Exp. Med.*, 64: 819–830, 1936. b. T. Shedlovsky and J. E. Smadel, *Jour. Exp. Med.*, 75: 165–178, 1942.

[40] J. E. Smadel and T. Shedlovsky, *Annals New York Acad. Sci.*, 43: 35–46, 1942.

[41] J. E. Smadel, T. M. Rivers and C. L. Hoagland, *Arch. Path.*, 34: 275–285, 1942.

[42] J. Casals and R. Palacios, *Jour. Exp. Med.*, 74: 409–426, 1941.

[43] J. Casals, *Am. Jour. Pub. Health*, 31: 1281–1284, 1941.

[44] E. C. Roberts and L. R. Jones, *Proc. Soc. Exp. Biol. and Med.*, 49: 52–54, 1942; *ibid.*, 47: 75–76, 1941.

[45] K. Goodner, SCIENCE, 94: 241–242, 1941.

[46] G. K. Hirst, SCIENCE, 94: 22–23, 1941.

[47] G. K. Hirst, *Jour. Exp. Med.*, 75: 49–64, 1942.

[48] G. K. Hirst and E. G. Pickels, *Jour. Immunol.*, 45: 273–283, 1942.

[49] F. P. O. Nagler, *Med. Jour. Australia*, 1: 281–283, 1942.

[50] A. B. Sabin, *Jour. Am. Med. Asn.*, 117: 267–269, 1941.

[51] E. W. Schultz, *Jour. Pediat.*, 20: 110–124, 1942.

While it is possible that the virus can multiply throughout the alimentary tract, the pharynx and small intestine appear to provide the sites of choice. The virus is believed to migrate from these areas to the central nervous system via two main routes.[52] The first, which gives rise to a preponderance of bulbar symptoms, is along the cranial nerves or the parasympathetic system into the medulla; the other, which results in paralysis of the extremities, is along the visceral afferent or efferent fibers of the intestine, through the corresponding spinal or abdominal sympathetic ganglia, into the spinal cord. The total inability to demonstrate a centrifugal spread of the virus from the central nervous system is interpreted to mean that the virus multiplies in, and is eliminated from, the alimentary tract. The persistence of the virus in the stools of convalescents,[53] its presence in the stools of healthy contacts,[53] the spread of the disease by healthy carriers[54] and perhaps by flies,[55] the occurrence of cases throughout the year with a peak incidence during the summer and early fall months all point to an epidemiologic picture typical of gastrointestinal rather than respiratory routes of infection.

The comprehensive studies of Howitt[56] have demonstrated that the viruses of western equine encephalomyelitis and of St. Louis encephalitis are endemic in central California. Hammon[57] has shown that epidemics due to both viruses can occur simultaneously and that human cases due to a mixed infection probably do occur. Both Howitt and Hammon and their associates have found that the sera of certain birds and mammals in the affected areas contain neutralizing antibodies to one or both of these viruses, a finding which not only points to a possible mechanism for widespread dissemination of the virus but also implies that an arthropod vector may be involved in transmission. Further, the complete lack of epidemiologic evidence that these viruses are carried through food or water or that infections arise through direct or indirect contact, as well as the limitation of these diseases to the warm months of the year are in accord with such a view. While *Triatoma sanguisuga* Leconte has been found[58] naturally infected with the western equine virus, its distribution does not coincide with that of the virus[59a] and it is believed by Hammon and his associates not to be an efficient vector.[59a] In a search for vectors possibly associated with the Yakima Valley outbreak of encephalitis Hammon *et al.*[60] isolated five strains of the western equine virus and three of the St. Louis virus—all from a single species of mosquito, *Culex tarsalis* Coquillet. This is the first instance of isolation of the St. Louis virus from any material other than human tissues, and the first time either virus has been found in a wild-caught mosquito. Since it does not necessarily follow that an arthropod infected with virus can transmit it, proof of ability to transmit must be obtained under experimental conditions. *C. tarsalis* was quickly proved capable of transmitting the St. Louis virus experimentally[59a] and *C. pipiens, C. coronator, Aedes lateralis, A. taeniorhynchus, A. vexans* and *Theobaldia incidens* have just been added[59b] as potential vectors. The western equine virus has been transmitted under experimental conditions by *C. tarsalis* and also by *Theobaldia incidens*.[59b]

We may find eventually that other arthropods can participate in the transmission of western equine encephalitis and St. Louis encephalitis since, under laboratory conditions, many Aedes as well as *Dermacentor andersoni* can transmit the western equine virus and *Dermacentor variabilis* can transmit the St. Louis virus (reviewed in[59a]).

One of the great riddles of epidemiology is what happens to a virus during interepidemic periods, when it apparently disappears, and what influences a virus to flare up suddenly from its quiescent state. A step toward the solution of this riddle is afforded by the important discovery of Shope[61] that the virus of swine influenza is capable of existence in a masked noninfectious form from which it can be provoked into activity by appropriate stimuli. Thus, in a swine with active influenza infection, the virus is taken up by lungworms (*Metastrongylus elongatus* and *Choerostrongylus pudendo-tectus*) in the lung. Embryonated ova are passed in the feces and eventually are ingested by an earthworm, which is the intermediate host of the lungworm. In the earthworm the ova pass through developmental cycles until the third larval stage, infective for pigs, is reached. Ingestion of infected earthworms by swine leads to liberation of the larvae

[52] A. B. Sabin, *Jour. Am. Med. Asn.*, 120: 506–511, 1942.

[53] a. S. D. Kramer, A. G. Gilliam and J. G. Molner, *Pub. Health Rep.*, 54: 1914–1922, 1939. b. S. D. Kramer, B. Hoskwith and L. H. Grossman, *Jour. Exp. Med.*, 69: 49–67, 1939. c. J. D. Trask, J. R. Paul and A. J. Vignec, *Jour. Exp. Med.*, 71: 751–763, 1940. d. H. A. Howe and D. Bodian, *Jour. Infect. Dis.*, 66: 198–201, 1940.

[54] E. A. Piszczek, H. J. Shaughnessy, J. Zichis and S. O. Levinson, *Jour. Am. Med. Asn.*, 117: 1962–1965, 1941.

[55] A. B. Sabin and R. Ward, SCIENCE, 94: 590–591, 1941; *ibid.*, 95: 300–301, 1942.

[56] a. B. F. Howitt, *Proc. Sixth Pacific Sci. Cong.*, 5: 235–245, 1942; b. B. F. Howitt and W. Van Herick, *Jour. Infect. Dis.*, 71: 179–191, 1942.

[57] W. M. Hammon, *Jour. Am. Med. Asn.*, 117: 161–167, 1941.

[58] C. H. Kitselman and A. W. Grundman, *Kansas Agric. Exp. Sta. Tech. Bull.* No. 50, p. 1–15, 1940.

[59] a. W. M. Hammon, W. C. Reeves, B. Brookman and C. M. Gjullin, *Jour. Infect. Dis.*, 70: 278–283, 1942. b. W. M. Hammon, W. C. Reeves and M. Gray, *Am. Jour. Pub. Health*, 33: 201–207, 1943.

[60] W. M. Hammon, W. C. Reeves, B. Brookman and E. M. Izumi, *Jour. Infect. Dis.*, 70: 263–266, 1942.

[61] R. E. Shope, *Jour. Exp. Med.*, 74: 41–47, 1941.

which make their way to the lungs and develop into adults. The virus continues to remain in its noninfective form until it is activated by a "provoking stimulus," such as repeated injections of *H. influenzae* or of calcium chloride, when the disease supervenes. What causes fully active swine influenza virus to become noninfective when taken up by the lungworm and to resume its infectivity when it again finds itself within a susceptible swine is still unknown. Shope has shown that the virus is able to survive for at least two years in its noninfective form in the lungworm, which indicates that the virus possesses an excellent means of ensuring its survival between epizootics.

PROPHYLAXIS AND THERAPY

An effective and relatively safe method of vaccination against yellow fever has been available since 1937[62a] when a strain (17D) of virus with attenuated virulence was obtained after prolonged tissue-culture passage of the classic Asibi strain. The vaccine, prepared from chick-embryo tissue infected with the 17D strain, has been used in endemic areas of yellow fever on such a huge scale and with such good results that its protective powers are undoubted (literature in[62b]).

Vaccines have also been developed against the eastern and western equine encephalomyelitis viruses, but in this case the high virulence of the viruses has required their inactivation with formol.[63] Their protective action in animals has been shown to be of a high order, and hence they probably exert a similar effect in man—at least no cases of the disease have occurred in vaccinated laboratory workers.[63]

Encouraging results are reported, in preliminary trials, with vaccination against the tick-borne Russian spring-summer encephalitis.[64] Formol-inactivated mouse brain virus suspensions were administered to 925 individuals in an endemic area. Two cases occurred in the vaccinated group and twenty-seven in the control group of 1,185 nonvaccinated individuals, ratios of 1 in 462 and 1 in 44, respectively.

The efficacy of vaccines against influenza A is still unknown and must await further trial under controlled conditions. A recent analysis by Horsfall[65] of five independent studies of the complex influenza A vaccine[66] showed that the reduction in incidence of the disease among vaccinated persons varied from 47 per cent. to practically nil, and that on the average the number of cases in the vaccinated group was about two thirds that of the unvaccinated group. In addition any increased resistance induced by vaccination seems to be of short duration.[67] Inhalations of immune serum have been reported to exert a protective action both in prophylaxis[68] and in therapy.[69]

The results of attempts at sulfonamide therapy in virus diseases have been disappointing. This is not surprising, however, since the presence of sulfonamides in tissue culture has been found to have no appreciable effect on the multiplication of any of the viruses cultivated in such an environment.[70,71] Of the diseases usually classed with those of virus origin, only four—trachoma, inclusion blenorrhea, lymphogranuloma venereum and mouse pneumonitis—are known to respond to sulfonamide therapy.[72] Rake, Jones and Nigg,[73] however, do not believe that the success in therapy in these four diseases has any bearing on the chemotherapy of the "true" virus disease, since there is increasing evidence[73,74] that the causative agents of the lymphogranuloma venereum-psittacosis group of diseases—to which these four belong[72]—should be separated from the true viruses.

NEW VIRUSES

New viruses and diseases caused by them continue to be uncovered. In 1938 a virus responsible for the Russian spring-summer type of encephalitis was recovered from the brains of fatal human cases by Levkovitsch, Shubladze, Chumakov and Soloviev.[75,76] The virus is transmitted to man by ticks (*Ixodes persulcatus*) and is reported[76] to be related immunologically to the virus of Japanese B, or summer, encephalitis, which is mosquito transmitted. Animals immune to the Russian spring-summer encephalitis virus are resistant to inoculation of the Japanese B virus and their sera neutralize completely the Japanese virus, but in the reverse direction only partial protection or neutralization occurs, which indicates that antigenically the Russian spring-summer encephalitis virus is more complex than the Japanese virus. Casals and

[62] a. M. Theiler and H. H. Smith, *Jour. Exp. Med.*, 65: 767–786, 1937. b. J. P. Fox and A. S. Cabral, *Am. Jour. Hyg.*, 37: 93–120, 1943.

[63] D. W. Beard, H. Finkelstein and J. W. Beard, *Jour. Immunol.*, 40: 497–507, 1941.

[64] A. A. Smorodintseff, N. W. Kagan, E. N. Levkovitsch and N. L. Dankovskij, *Arch. ges. Virusforsch.*, 2: 1–25, 1941.

[65] F. L. Horsfall, Jr., *Jour. Am. Med. Asn.*, 120: 284–287, 1942.

[66] F. L. Horsfall and E. H. Lennette, SCIENCE, 91: 492–494, 1940.

[67] G. K. Hirst, E. R. Rickard, L. Whitman and F. L. Horsfall, Jr., *Jour. Exp. Med.*, 75: 495–511, 1942.

[68] R. M. Taylor, *Jour. Immunol.*, 41: 453–462, 1941.

[69] A. A. Smorodintseff, *Proc. Third Int. Cong. Microbiol.*, New York, September 2–9, 1939, p. 375 (abstract).

[70] M. Sanders, C. H. Huang and H. S. Simms, *Jour. Bact.*, 45: 81–82, 1943 (abstract).

[71] H. Koprowski and E. H. Lennette, *Am. Jour. Hyg.*

[72] G. Rake, M. F. Shaffer and P. Thygeson, *Proc. Soc. Exp. Biol. and Med.*, 49: 545–547, 1942.

[73] G. Rake, H. P. Jones and C. Nigg, *Proc. Soc. Exp. Biol. and Med.*, 49: 449–452, 1942.

[74] M. D. Eaton, W. P. Martin and M. D. Beck, *Jour. Exp. Med.*, 75: 21–33, 1942.

[75] E. N. Levkovitsch, A. K. Shubladze, M. P. Chumakov and V. D. Soloviev, *Arch. Sc. Biol.*, 52: 162–163, 1938.

[76] A. A. Smorodintseff, *Arch. ges. Virusforsch.*, 1: 468–480, 1940.

Webster[77] have reported that preliminary cross-fixation and cross-immunity tests indicate the Russian spring-summer virus to be very closely related to, if not identical with, louping-ill virus which, also transmitted by ixodid ticks, is the cause of an encephalitis in sheep in Scotland and may have been responsible for an outbreak of human encephalomyelitis (X-disease) in Australia in 1917–18.[78] If the close relationship of the Russian spring-summer encephalitis and louping-ill viruses is substantiated, one might speculate as to whether the Japanese B virus may not represent a variant of these viruses arising from prolonged association with another arthropod vector. As a matter of fact, the virus causing the Russian autumn encephalitis has been identified as that of Japanese B encephalitis, and has been recovered from naturally infected *Culex pipiens* and *C. tritaeniorhynchus*.[79]

Isolation of the West Nile virus was reported in 1940 by Smithburn, Hughes, Burke and Paul.[80] The name derives from the locality (West Nile district, Northern Province of Uganda) from which the blood specimen containing the virus was furnished, and as the specimen was taken during the course of a routine sleeping sickness survey, nothing is known of the pathologic activity of this virus in man. It has, however, some relationship to the viruses producing encephalitides in man, since it is neutralized by immune sera to both the St. Louis and Japanese B viruses, although its corresponding immune sera lack any demonstrable capacity to neutralize these viruses.[81]

Smithburn, Mahaffy and Paul[82] in 1941 reported the isolation on different occasions of a virus associated with an illness whose only features were abrupt onset, fever and severe headache and backache—the disease has been named Bwamba fever after the county in the Western Province of Uganda where it occurred.

In a number of outbreaks of undoubted influenza it proved difficult or impossible to demonstrate that the etiologic agent was the classic influenza virus, now known as influenza A virus.[83] An explanation in part was provided in 1940 when Magill[84] and Francis[85] independently and almost simultaneously announced the isolation of a second influenza virus, now designated influenza B.[83, 85] While these viruses are completely distinct immunologically, the infections they produce can not be distinguished clinically one from another. Since these viruses, alone or together, fail to account for a considerable number of cases, depending on the epidemic, it is reasonable to assume the existence of additional influenza viruses as yet unrecognized.[86]

During the last few years there has been observed with increasing frequency a respiratory disease known by several names but usually referred to as atypical pneumonia (reviewed in [87]). A number of viral agents whose association with the disease is sometimes difficult to assess and whose relationship to each other is still indeterminate, have been isolated.[88] Of these agents the best known and most completely studied is the virus isolated by Eaton, Beck and Pearson[88c] in 1940 and called meningopneumonitis virus because of its close antigenic similarity to the meningopneumonitis virus isolated in 1938 by Francis and Magill[89] from ferrets inoculated with human throat washings and believed by them to have been present in their normal ferret stock. Recently acquired evidence[88c, 90] shows that the viruses of meningopneumonitis, lymphogranuloma venereum and psittacosis are related antigenically, and in addition are characterized by the formation of elementary bodies with similar tinctorial properties and by their ability to produce meningitis, pneumonia and granulomata in the skin of suitable test animals. So similar are these viruses in their properties that it appears not improbable that they are derived from a common progenitor and that by adaptation to different tissues and animal species they have acquired certain characteristics peculiar to themselves. Eaton *et al.*[88e] have recently isolated another virus-like agent from cases of atypical pneumonia and it will be interesting to know whether the new agent will fall into the lymphogranuloma venereum-psittacosis group.

During the summer of 1941 there occurred in Oahu,

[77] J. Casals and L. T. Webster, SCIENCE, 97: 246–248, 1943.

[78] a. F. M. Burnet, *Med. Jour. Australia*, 1: 679–681, 1934. b. J. R. Perdrau, *Jour. Path. and Bact.*, 42: 59–65, 1936.

[79] A. A. Smorodintseff, A. K. Shubladse and V. D. Neustroev, *Arch. ges. Virusforsch.*, 1: 549–559, 1940.

[80] K. C. Smithburn, T. P. Hughes, A. W. Burke and J. H. Paul, *Am. Jour. Trop. Med.*, 20: 471–492, 1940.

[81] K. C. Smithburn, *Jour. Immunol.*, 44: 25–31, 1942.

[82] K. C. Smithburn, A. F. Mahaffy and J. H. Paul, *Am. Jour. Trop. Med.*, 21: 75–90, 1941.

[83] F. L. Horsfall, Jr., E. H. Lennette, E. R. Rickard, C. H. Andrewes, Wilson Smith and C. H. Stuart-Harris, *Lancet*, 2: 413, 1940.

[84] T. P. Magill, *Proc. Soc. Exp. Biol. and Med.*, 45: 162–164, 1940.

[85] T. Francis, Jr., SCIENCE, 92: 405, 1940.

[86] E. H. Lennette, E. R. Rickard, G. K. Hirst and F. L. Horsfall, Jr., *Pub. Health Rep.*, 56: 1777–1788, 1941.

[87] J. H. Dingle and M. Finland, *New England Jour. Med.*, 227: 378–385, 1942.

[88] a. J. Stokes, Jr., A. S. Kenney and D. R. Shaw, *Tr. & Stud. College Physicians, Philadelphia*, 6: 329–333, 1939. b. J. M. Weir and F. L. Horsfall, Jr., *Jour. Exp. Med.*, 72: 595–610, 1940. c. M. D. Eaton, M. D. Beck and H. E. Pearson, *Jour. Exp. Med.*, 73: 641–654, 1941. d. J. A. Baker, SCIENCE, 96: 475–476, 1942. e. M. D. Eaton, G. Meiklejohn, W. Van Herick and J. C. Talbot, SCIENCE, 96: 518–519, 1942.

[89] Thomas Francis, Jr. and T. P. Magill, *Jour. Exp. Med.*, 68: 147–163, 1938.

[90] M. D. Eaton, W. P. Martin and M. D. Beck, *Jour. Exp. Med.*, 75: 21–33, 1942.

Hawaii, a large outbreak of a highly contagious, acute type of conjunctivitis.[91] By September the epidemic, which is thought to have had its origin in Malaya,[92] had spread to the Pacific Coast of the United States, where it involved chiefly shipyard workers. In the late summer and early fall of 1942 outbreaks of the disease occurred in New York, Schenectady and Hartford.[92] From cases in the New York outbreak of the disease, now designated epidemic keratoconjunctivitis, Sanders and Alexander[93] were able on two occasions to isolate in tissue culture a virus which has proved to be pathogenic for man and for mice and rabbits. The association of their virus with the human disease appears to be established, although further work is desirable and doubtless will be forthcoming.

In conclusion, it should be emphasized that this presentation has of necessity been limited in scope and that many interesting and important contributions to our knowledge of viruses have had, perforce, to be omitted. So intensively and so sedulously have viruses and the diseases due to them been studied in recent years that any attempt, such as this, to summarize briefly the recent advances in this field, can do no more than present the high lights.

[91] Editorial, *Jour. Am. Med. Asn.*, 118: 460, 1942.

[92] J. H. Dunnington, *Symposium on Epidemic Keratoconjunctivitis* held at the College of Physicians and Surgeons, Columbia University, School of Medicine, under the direction of the Division of Preventive Medicine, Office of the Surgeon General, Department of War, and in conjunction with the Commission on Neurotropic Virus Diseases, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, December 4, 1942.

[93] M. Sanders and R. C. Alexander, *Jour. Exp. Med.*, 77: 71–95, 1943.

OBITUARY

FELIX AGUILAR

THE director of the Astronomical Observatory of the University of La Plata, Dr. Félix Aguilar, died suddenly on September 28, 1943. Mr. Aguilar was not only one of the leading astronomers of the Republic of Argentina, but he was also active as president of the Comisión para la Medición de un arco de meridiano en la República Argentina, president of the Comisión Nacional de Observatorios and member of the Comisión de límites Argentino-Chilena. He served as professor of geodesy in the University of La Plata and was a member of several scientific associations such as the Sociedad Científica Argentina and the Academia Nacional de Ciencias. At the La Plata Observatory his name was connected with the creation of the Escuela Superior de Ciencias Astronómicas y Conexas and with the Instituto Geográfico Militar, where he served as head of the geodesy department. He was active in the determination of the difference in longitude between Potsdam and Belgrano (Buenos Aires), and participated in the first gravimetrical and magnetic investigations of the Instituto Geográfico. In 1936 he was placed in charge of the reorganization of the Observatorio Astronómico Nacional at Córdoba. He was the author of many scientific papers and invented a method for the use of calculating machines in the determination of latitude by a method of Gauss. He undertook one of the few astronomical leveling operations that have ever been executed. A short time before his death he arranged for two of his associates, Dr. Carlos Cesco and Dr. Jorge Sahade, to come to the United States for research in astrophysics.

OTTO STRUVE

DEATHS AND MEMORIALS

DR. ALEXANDER G. MCADIE, from 1913 to 1931 professor of meteorology at Harvard University and for eighteen years director of the Blue Hill Observatory, died on November 1 at the age of eighty years.

DR. HENRY VINECOME ARNY, who retired in 1937 as dean of the College of Pharmacy of Columbia University, died on November 3. He was seventy-five years old. Dr. Arny had served as professor of chemistry at the College of Pharmacy from 1911 to 1937 and as dean of the college from 1930 to 1937.

DR. GLENN WARREN GOLDSMITH, since 1929 professor of botany and bacteriology at the University of Texas, died on October 28. He was fifty-six years old.

DR. IRA EDWARDS, curator in geology of the Milwaukee Museum, died on October 31 at the age of fifty years.

CHARLES A. DONNEL, a former head of the Office of the U. S. Weather Bureau in Chicago, principal meteorologist and supervising forecaster for the district, died on October 29. He was sixty-two years old.

A CORRESPONDENT writes: Dr. Wilmon Newell, provost for agriculture at the University of Florida, director of the Agricultural Experiment Station and Extension Service, and plant commissioner, State Plant Board, as already reported in SCIENCE, died on October 25 at the age of sixty-five years. After serving as entomologist in Iowa, Ohio, Texas, Georgia and Louisiana, he accepted the position of plant commissioner in 1915 with the newly created State Plant Board and directed the campaign which eradicated citrus canker in Florida. In 1929 he directed a similar campaign for the eradication of the Mediterranean fruit-fly; this work was completed in 1930. He was

director of the Florida Agricultural Experiment Station and Extension Service from 1921 to date, dean of the College of Agriculture from 1921 to 1938 and provost for agriculture since 1938.

MEMORIAL exercises in honor of the late Dr. Frank Schlesinger, professor of astronomy and director of Yale University Observatory, emeritus, who died on July 10, will be held in Strathcona Hall, Yale University, on Friday, November 19, at 4:30 P.M. The speakers will be Dr. James Rowland Angell, president emeritus of Yale University, and Professor Henry Norris Russell, of Princeton University. President Charles Seymour, of Yale University, will preside.

A PERMANENT memorial to William Beaumont, known as the founder of our modern knowledge of the physiology of the stomach, has been assured by the transfer of the historical "Early House" on Mackinac Island to public ownership.

SCIENTIFIC EVENTS

GIFTS TO THE ROYAL COLLEGE OF SURGEONS, ENGLAND

AN immediate gift of £100,000 for the endowment of the department of pathology and the institution of a chair of human and comparative pathology to the Royal College of Surgeons of England by W. H. Collins, of Buckinghamshire, is reported in *The Times*, London.

Mr. Collins has also informed the college that he has made provision in his will for a bequest of a further £100,000 for the endowment of the department of anatomy and the institution of a chair of human and comparative anatomy.

Sir Alfred Webb-Johnson, who presided at a meeting of the council of the college, when the gifts were announced on October 14, read a letter from Mr. Collins, in which he said:

> Throughout my career I have realized how essential is the study and investigation of basic problems. Success of armies in the field is dependent on careful planning and preparation at headquarters, and victories in the war against disease can only be achieved by due application and increased knowledge of the fundamental medical sciences.
>
> I have been greatly impressed with the value of the departments of anatomy and pathology, which have made the Royal College of Surgeons of England famous all over the world. I have seen what grievous injury your departments have suffered as the result of enemy action, and appreciate what a gigantic task it will be to restore them to their unique position in the scientific world. To embark upon this task it is essential that the departments shall have an assured income from endowments. . . . I trust that my gifts will enable the council to proceed with confidence with their responsible task and to engage the services of men of outstanding ability to assist them in their labors.

It is recalled in *The Times* that the Royal College of Surgeons was badly damaged in the air raids in 1941 and that most of the Hunterian collection was lost when the museum of the college, situated in Lincoln's Inn Fields, was wrecked by a high-explosive bomb. The museum was unique and the Hunterian collection was the proudest possession of the college.

REPORT OF THE COMMITTEE ON THE PROFESSIONAL TRAINING OF CHEMISTS

THE Committee on the Professional Training of Chemists, according to *Chemical and Engineering News*, has had inquiries as to the minimum time required for a student in chemistry to complete his professional training in an accelerated program—especially as to whether it would be possible to complete the requirements of the society in two calendar years. The maximum time now allowed by Selective Service for deferment of students of chemistry and of other fields of technology is twenty-four months. It is the opinion of the committee that the present requirements can not be met in less than two and two-thirds calendar years, which would include eight semesters in an accelerated tri-semester schedule.

At present freshman and sophomore students become eighteen years of age before they are within twenty-four months of graduation and can not be deferred. The stream of technical students is therefore drying up at the source. Already the enrolment is down to about one third of normal. Unless some provision is made for a longer period of deferment for chemists and engineers, within one or two more years there will be no fully trained graduates in these technical fields.

It is further the opinion of the committee that students who take the Army specialist training courses in chemical engineering or other essential fields should return to college later to complete the standard requirements in order to prepare themselves to be permanently useful in industry or to go on in advanced training.

W. A. NOYES, JR., *Chairman*
E. M. BILLINGS
S. C. LIND
H. B. WEISER
W. G. YOUNG

THE DYSENTERY REGISTRY

THE present military situation and the general increasing interest in bacillary dysentery has resulted in many inquiries concerning the work of the Dysentery Registry. The organization was founded in 1933 for the prevention and study of bacillary dysentery. It was found that when cases of infectious diarrhea as a whole were carefully studied, most of them appeared to be bacillary dysentery. Greater interest in the recognition of bacillary dysentery and an actual rising incidence of the disease in the United States resulted in a forty-fold increase in the number of reported cases between the years 1933 and 1941. Major advances in bacillary dysentery have occurred during this period. A seven-point program for the control of the disease was formulated in 1933 and was largely responsible for the compulsory reporting of bacillary dysentery in all states by 1940 (it had not been a reportable disease in 15 states in 1937).

As part of the educational program, a film entitled "Hand to Mouth" (800 feet, 16 mm silent) was produced for the New York World's Fair. Since then copies of the film have been loaned, without cost, to public health and educational agencies throughout the United States and South America. Others have been purchased at actual cost by the American Medical Association and many of our state and city health departments. A permanent copy is on file at the Wistar Institute.[1]

The registry has received the cooperation of government officials throughout the world, and has, in turn, given freely of its accumulated knowledge and resources.

Since the outbreak of the second world war, the work of the Dysentery Registry in furnishing strains or diagnostic sera and in the identification of atypical organisms for public health and military laboratories has greatly increased. Preliminary tests during the past two months indicate the wide applicability in the United States of the Boyd strains and of the new classification of the dysentery group of organisms.

Regional branches of the registry are now in process of formation throughout the world, chiefly at universities and departments of health. The present membership roster includes most of the prominent investigators in the field, chiefly associated with universities and government public health agencies. The central registry has been supported by the Bronx Hospital and by the voluntary contributions of friends of the registry (Blood Betterment Association, Schonbrunn and Golding Funds). Although available funds are very limited, economical management has made possible the rendering of all services without cost to those who seek them. There is every reasonable expectation that the problem of bacillary dysentery and the other infectious diarrheas will increase during the war and post-war periods.

[1] Reviews of Approved Films in Anatomy and Biology, *Anatomical Record.*

JOSEPH FELSEN, M.D.,
Director, Dysentery Registry
THE BRONX HOSPITAL,
NEW YORK, N. Y.

RARE CHEMICALS

THE following chemicals are wanted by the National Registry of Rare Chemicals, Armour Research Foundation, 33rd, Dearborn and Federal Streets, Chicago, Ill.:

p-Aminophenylalanine
Berberine hydrochloride
Decamethylenediguanidine
Ergothionine
Iodoacetic acid (large quantities)
Laevo butandiol-2,3
Methyl silican chlorides (CH_3) Si Cl_3 or $(Ch_3)_2$ Si Cl_2
Nickel tetra carbonyl
Pseudo-ionone
Piperonylidine acetophenone
Sodium sulfadiazine
Trimethyl sulphine hydroxide $(CH_3)_3$ S–OH
Thiolhistidine
2-Thioparabanic acid
Vinyl ethyl ether
Vinyl stearate
Xanthopterin

PROGRAM OF THE LANCASTER BRANCH OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

THE Lancaster Branch of the American Association, which has approximately a thousand members, has announced the following lecturers with their subjects for the season 1943 to 1944:

November 11, Dr. David Sarnoff, president of the Radio Corporation of America, "Industrial Science Looks Ahead."

December 9, The Rev. Bernard R. Hubbard, S.J., geologist at Santa Clara University and well-known lecturer, "The Aleutian Battleground."

January 13, Albert Q. Maisel, war correspondent, "Miracles of Military Medicine."

February 17, Dr. Kirtley F. Mather, professor of geology at Harvard University, "Natural Resources and World Organization."

March 30, Larry F. Livingston, manager of the Agricultural Extension Division of the E. I. du Pont de Nemours and Company, "Yesterday, To-day and To-morrow."

Officers of the branch are: Jaques Cattell, *Chairman;* Dr. C. C. Vogt, *Vice-chairman;* Dr. Frances A. Coventry, *Secretary,* and Professor H. M. Fry, *Treasurer,*

THE PACIFIC DIVISION OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

AT the meeting of the executive committee of the Pacific Division of the American Association for the Advancement of Science, held on October 15, it was agreed that meetings of the division be suspended for the duration of the war. The secretary was instructed to notify all affiliated and associated societies to this effect and to offer the services of his office in facilitating the arrangements of small regional meetings by individual societies or by such groups of societies as may desire to hold meetings. The action of the executive committee resulted from a poll of member societies and from consideration of the increasing difficulties in transportation and housing which render difficult the holding of scientific meetings of any appreciable size.

In order to maintain the necessary contacts with member societies and to facilitate the initiation of meetings at the end of this emergency, Dr. J. Murray Luck, professor of biochemistry at Stanford University, secretary of the division, should be advised of any changes in secretaryship that may occur in affiliated and associated societies.

THE AMERICAN PHILOSOPHICAL SOCIETY

THE autumn general meeting of the American Philosophical Society, Philadelphia, will be held on November 19 and 20. The following program has been arranged:

FRIDAY MORNING, NOVEMBER 19

Open Session, 10 o'clock

Edwin G. Conklin, president, in the chair.

Victor F. Hess,[1] professor of physics, Fordham University, "A Study of the Ionization of the Atmosphere by Cosmic and Local Radiation." (Lantern slides.)

William H. Hobbs,[1] professor emeritus of geology, University of Michigan, "The Scablands Glacial Lobe in Eastern Washington." (Lantern slides.)

Albert F. Blakeslee,[1] director, Genetics Experiment Station, Smith College, and Sophie Satina, "New Hybrids from Incompatible Crosses in Datura through Culture of Excised Embryos on Malt Media." (Lantern slides.)

John E. Weaver,[1] professor of plant ecology, University of Nebraska, "Recovery of Midwestern Prairies from Drought." (Lantern slides.) (To be read by Elmer D. Merrill.)

Charles B. Davenport, research associate (ret.), Carnegie Institution of Washington, "Periodicity in Growth of Long Bones." (Lantern slides.)

Alexander Sandow,[1] assistant professor of biology, Washington Square College of Arts and Science, "Latency-Relaxation and Mechano-Chemical Coupling in Muscular Contraction." (Lantern slides.)

[1] Recipient of grant from the Research Funds.

Carl C. Speidel,[1] professor of anatomy, University of Virginia, "A Cine-Photomicrographic Study of the Activities of Lymph Vessels and Macrophages in the Disposal of Extravasated Red Blood Cells." (Lantern slides and moving pictures.)

John H. Storer,[1] Waltham, Mass., "Study of the Soaring Technique of the California Condor." (Lantern slides and moving pictures.)

Luncheon for members and invited guests, 1 o'clock.

FRIDAY AFTERNOON

Open Session, 2 o'clock

Symposium on the Organization, Direction and Support of Research

George Howard Parker in the chair.

Hugh S. Taylor, David B. Jones professor of chemistry, Princeton University, "Research in the Physical Sciences."

Detlev W. Bronk, professor of biophysics, director, Eldridge Reeves Johnson Foundation for Medical Physics, University of Pennsylvania, "The Discovery and Interpretation of Biological Phenomena."

Alan Gregg, director for the Medical Sciences, Rockefeller Foundation for Medical Research, "Medical Research."

Open Discussion

To be led by Karl K. Darrow, research physicist, Bell Telephone Laboratories.

FRIDAY EVENING, 8:30 O'CLOCK

Edwin G. Conklin, president, in the chair.

Franklin Medal Lecture

James B. Conant, president, Harvard University, "The Advancement of Learning in the United States in the Post-War World." The lecture will be followed by a reception.

SATURDAY MORNING, NOVEMBER 20

Open Session, 10:30 o'clock

Edward P. Cheyney, vice-president, in the chair.

Harold A. Innis, professor of political economy, University of Toronto, "Political Economy in the Modern State."

Robert Livingston Schuyler, Gouverneur Morris professor of history, Columbia University, "War and Historiography."

Marjorie Hope Nicolson, professor of English, Columbia University, "Merchants of Light: Research in Arts and Letters."

Open Discussion

To be led by Roy F. Nichols, professor of history, University of Pennsylvania.

Luncheon for Members and Invited Guests, 1 o'clock.

SATURDAY AFTERNOON

Open Session, 2 o'clock

W. F. G. Swann, secretary, in the chair.

William Berryman Scott,[1] professor emeritus of geology, Princeton University, "Vertebrate Fossils of the Duchesne River Beds."

Edwin Walter Kemmerer, professor emeritus of interna-

tional finance, Princeton University, "The International Character of Economics."

Lloyd R. Watson,[1] professor of chemistry, Alfred University, "Economic Aspects of Controlled Mating of Honeybees."

Charles R. Anderson,[1] associate professor of American literature, the Johns Hopkins University, "The Centennial Edition of Sidney Lanier."

Charles de Tolnay,[1] Institute for Advanced Study, "Theory of Drawing in Italy and France During the Renaissance and Baroque."

THE CHARLES L. MAYER AWARD OF THE NATIONAL ACADEMY OF SCIENCES

MANUSCRIPTS and published articles submitted for the 1943 Charles L. Mayer Prize are being received by the National Science Fund of the National Academy of Sciences, 515 Madison Ave., New York 22, N. Y. The closing date for the receipt of contributions is January 15, 1944.

The award will be made for an outstanding contribution to present-day knowledge of factors affecting the growth of animal cells with particular reference to human cancer, and the advisory committee assisting the National Science Fund in administering the award is prepared to consider contributions published during 1943 or in manuscript. In addition, the committee requests recommendations from scientists or persons whose present work comes within the field for which the award is offered and who are achieving outstanding results.

The donor of the Charles L. Mayer Award had in mind the vast possibilities offered for research on the action of chemical agents and physical factors in stimulating or retarding cell growth, and the committee is interested primarily in fundamental studies on the factors influencing the growth of animal cells rather than applications to any particular aspect of normal or abnormal growth. The 1942 award was made to Dr. Charles Huggins, of the University of Chicago, for his work on endocrine control of prostatic cancer.

The advisory committee in charge of recommendations for the 1943 Charles L. Mayer Award includes Dr. Alan Gregg, director for the medical sciences, Rockefeller Foundation; Dr. George H. Whipple, dean of the School of Medicine and Dentistry of the University of Rochester; Dr. Peyton Rous, the Rockefeller Institute for Medical Research; Dr. R. R. Williams, chemical director of the Bell Telephone Laboratories, and Elihu Root, Jr.

SCIENTIFIC NOTES AND NEWS

THE autumn meeting of the National Academy of Sciences will be held in the Academy Building, Washington, D. C., on Monday, November 22. Registration will be at 9 A.M. The meeting will be for members only. It will be confined to academy business and reports from members who are actively engaged in the war effort. It is expected that the session will be limited to one day, beginning at 9:30 A.M. Luncheon, limited to members, will be at 1 P.M. at the Roger Smith Hotel.

THE Board of Directors of City Trusts of Philadelphia announces the conferring of the John Scott Awards on Dr. Otto Stader, veterinary surgeon, Ardmore, Pa., for the invention of the reduction and fixation bone splint; on John C. Garand, chief engineer of ordnance, Springfield Armory, for the invention of the U. S. Rifle Cal. .30 M. 1, and, as already announced in SCIENCE, on Dr. Richard E. Shope, of the Rockefeller Institute for Medical Research at Princeton, N. J., Lieutenant Commander, U. S. Naval Reserve, for the discovery of the complex etiology of swine influenza. The awards will be presented on Thursday evening, November 18, at 8:30 o'clock in the Hall of the American Philosophical Society.

DR. FREDERICK L. HOFFMAN, of the Biochemical Foundation of the Franklin Institute, now retired and living in San Diego, Calif., who was influential thirty years ago in founding the American Society for the Control of Cancer, was on November 2 at the seventeenth annual dinner of the New York City Cancer Committee awarded *in absentia* the "Clement Cleveland Award for 1943." The medal, which is presented annually "for outstanding service in the cause of cancer control," was accepted for Dr. Hoffman by Dr. Howard C. Taylor, attending surgeon at the Roosevelt Hospital. The presentation was made by Mrs. Robert G. Mead, daughter of the late Dr. Cleveland, in whose memory the award was established. This year's dinner of the New York Committee was given in honor of the founders of the American Society for the Control of Cancer. Dr. Clarence C. Little, managing director, reviewed the history of the organization. There was an exhibit showing the advance in cancer control that has taken place during the past thirty years.

THE Philadelphia College of Pharmacy and Science conferred at commencement on November 3 the degree of doctor of science on Dr. Theodore G. Klumpp, president of the Winthrop Chemical Company, in recognition of "distinguished services in medicinal chemistry."

DR. CURTIS SAUNDERS, master sergeant, division of

parasitology and tropical medicine of the Army Medical School, Washington, D. C., was elected on October 12 a member of the Royal Institute of Public Health and Hygiene, London.

DR. LEASON H. ADAMS, director of the Geophysical Laboratory of the Carnegie Institution of Washington, has been nominated as president-elect of the American Chemical Society.

DR. HENRY T. HEALD, president of the Illinois Institute of Technology, was elected president of the Association of Urban Universities at its twenty-ninth annual meeting in Chicago; Dr. David D. Henry, executive vice-president of Wayne University, was elected vice-president. Dr. F. W. Shockley, director of the extension and evening divisions and of the summer session of the University of Pittsburgh, will continue as secretary-treasurer.

F. MALCOLM FARMER, vice-president and chief engineer of the Electrical Testing Laboratories, has been elected president of the United Engineering Trustees, Inc., the joint agency of the four national societies of civil, mining and metallurgical, mechanical and electrical engineers.

CLYDE G. CONLEY, of the Mt. Vernon Bridge Company, Ohio, has been elected president of the American Institute of Steel Construction.

GEORGE ROBERTS, head of the department of agronomy of the University of Kentucky and agronomist at the experiment station for nearly forty years, retired on July 1 with the title professor of agronomy emeritus. He has been succeeded by Edmund J. Kinney, professor of farm crops and agronomist in charge of tobacco and cereal investigations.

IT is reported in the *Journal* of the American Medical Association that Dr. Harold W. Brown has resigned as dean of the School of Public Health of the University of North Carolina, to become professor of parasitology in the newly established department of tropical medicine of the Columbia Presbyterian Medical Center. He is also the first member of the faculty for training and research in tropical diseases, which will function under the immediate direction of the DeLamar Institute of Public Health, a division of the medical school. The project was made possible by a grant of $150,000 from the Josiah Macy Jr. Foundation, which will also defray a concentrated five-year program of research and teaching.

DR. PAUL HERGET, absent on leave from the Observatory of the University of Cincinnati to fill a war position at the U. S. Naval Observatory, Washington, has been appointed director of the observatory at Cincinnati. He succeeds the late Dr. Elliott Smith, who died on September 29. Dr. Everett I. Yowell, professor emeritus of astronomy, will continue as acting director until Dr. Herget can be released by the Naval Observatory.

RONALD MARTIN FOSTER, until recently a research mathematician in the Bell Telephone System, has joined the faculty of the Polytechnic Institute of Brooklyn as head of the department of mathematics.

LOWELL E. WALTERS, instructor in animal industry at the Louisiana State University, has been appointed assistant professor of animal husbandry at the Massachusetts State College.

DR. ROBERT I. WISE, formerly director of the Public Health Laboratory of Houston, Texas, has become assistant professor of bacteriology in the Medical School of the University of Texas. Dr. Glenn Drager, formerly of the department of anatomy of the Medical School of the West Virginia University, has been appointed assistant professor of anatomy.

FREDERIC H. MILLER, associate professor of mathematics and acting head of the department at Cooper Union, New York, has been appointed professor of mathematics and head of the department. He succeeds Professor H. W. Reddick, who has resigned.

DR. WILLIAM A. HOOKER, senior economic zoologist of the U. S. Department of Agriculture, has retired after serving for forty years.

C. KENNETH BULLOCK, Chautauqua County, N. Y., agricultural agent since 1930, has been appointed assistant secretary to Earl C. Foster, executive secretary of the New York State Emergency Food Commission.

DR. EDWARD I. SALISBURY, known for his work in tropical medicine, has been made medical director of the United Fruit Company to succeed Dr. Roland C. Connor, executive vice-president.

DR. J. C. HOSTETTER has resigned as vice-president and director of research and development of the Hartford Empire Company, Connecticut, to become president of the Mississippi Glass Company, St. Louis.

THE War Department, Washington, D. C., announced on October 21 the appointment of Colonel Stanhope Bayne-Jones, M. C., A.U.S., as director of the United States of America Typhus Commission. According to the *Journal* of the American Medical Association, Colonel Bayne-Jones succeeds Brigadier General Leon A. Fox, U. S. Army, who asked to be relieved as director and appointed field director in order to give all his time to the field work of the commission, which has been operating abroad, particularly in the Middle East, since the first of this year. Colonel Bayne-Jones takes over the directorship in addition to his work as assistant director of the Preventive

Medicine Division, Office of the Surgeon General, where the main office of the commission has been established. Colonel Bayne-Jones was formerly dean of the Yale University School of Medicine and was professor of bacteriology when ordered to active duty early in 1942.

FOLLOWING the death of Dr. Wilmon Newell, provost for agriculture at the University of Florida, director of the Agricultural Experiment Station and Extension Service, plant commissioner, State Plant Board, the following appointments, effective on November 1, have been announced: H. Harold Hume, dean of the College of Agriculture, provost for agriculture and dean of the College of Agriculture; Associate Director Harold Mowry, director of the Agricultural Experiment Station, and Associate Director A. P. Spencer, director of the Agricultural Extension Service. Assistant State Plant Commissioner A. C. Brown has been appointed plant commissioner to succeed Dr. Newell. The plant board is not connected with the University of Florida. The appointment by the Board of Control of Dr. P. J. Westgate as associate horticulturist, for duty with the Sub-Tropical Experiment Station, Homestead, was also announced.

THE *Experiment Station Record* reports that Dr. A. L. Deering, dean of the College of Agriculture of the University of Maine and director of the extension service, has also been given supervision over the Experiment Station in a program to coordinate the three branches of agriculture in the university. Because of the decreased student enrolment, several members of the college faculty have been transferred temporarily to the station for research on a full-time or a part-time basis. Dr. Arthur Hawkins, assistant agronomist of the station, has resigned to accept an appointment with the Bureau of Plant Industry, Soils and Agricultural Engineering of the U. S. Department of Agriculture, but will remain in Maine to carry on research in cooperation with the station.

DR. D. T. MACDOUGAL, of Mt. Carmel, Calif., has resigned as a member of the Board of Managers of the New York Botanical Garden. He is succeeded by Edwin De T. Bechtel. The *Bulletin* of the garden states that Dr. MacDougal's association with the garden began in 1899 when he was appointed director of the laboratory and first assistant. In July, 1904, he was made assistant director, continuing also in charge of the laboratory until he severed his connection at the end of 1905. From 1929 until 1933, he was one of its scientific directors, and was then elected to the board of managers. Dr. MacDougal has been a member of the corporation since the beginning of 1930.

DR. BASSETT MAGUIRE, who returned to New York in August after a summer spent exploring in the mountains of Utah and western Nevada, has been appointed non-resident professor of botany at the Utah State Agricultural College, where he taught for twelve years before accepting his appointment as curator at the New York Botanical Garden, in recognition of services rendered to the college.

DR. JOHN J. BOURKE, regional medical officer attached to the New York Regional Office of Civilian Defense, has been promoted from the rank of major in the U. S. Public Health Service to that of lieutenant colonel. He was formerly chief medical officer for the New York State War Council.

DR. OSCAR IVANISSEVICH, professor of surgery and director of the Surgical Institute at the University of Buenos Aires, exchange professor of surgery at Stanford University for the months of October and November, will give the Morris Herzstein Medical Lectures for 1943 in San Francisco on November 15, 17 and 19. He will speak on "Echinococcosis." The Herzstein Lectures were established in 1929 by the late Dr. Morris Herzstein, of San Francisco, to be given under the direction of the medical schools of Stanford University and the University of California. They are given on alternate years by scientific men of outstanding achievement and are open to the public as well as to the medical profession.

IT is reported in *Nature* that the Parsons Memorial Fund, which is administered by the Royal Society, made provision for a memorial to the late Honorable Sir Charles Parsons in Westminster and for an annual Parsons Lecture to be given in turn under the auspices of eight specified institutions and societies, concerned with the subjects most closely associated with his name. In accordance with the terms governing the appointment of the lecturers, the 1943 lecture, which is the eighth of the series, was given under the auspices of the Physical Society. It was delivered at the meeting of the society at the Royal Institution, on October 15, by the Right Honorable Lord Rayleigh, whose subject was "Optical Topics, in Part Connected with Charles Parsons." Previous lecturers have dealt more especially with other aspects of his work.

BECAUSE of information received that it will not be possible for St. Louis to provide adequate hotel accommodations, the date of the meeting of the annual session of the American Medical Association, which had been scheduled to be held in St. Louis, has been changed by the Board of Trustees. It will now be held in Chicago from June 12 to 16.

THE spring convention of the Electrochemical Society will be held at Milwaukee from April 12 to 15, 1944.

THE forty-ninth summer meeting of the American Mathematical Society and the twenty-fifth colloquium were held in September at the New Jersey College for Women, Rutgers University. The Mathematical Association of America and the Institute of Mathematical Statistics met in conjunction with the society. There was an attendance of about three hundred, including two hundred and forty-two members of the society. The program consisted of three colloquium lectures on "Existence Theorems in the Calculus of Variations," by Professor E. J. McShane; two addresses, "The Complex Method of the Theory of Trigonometric Series," by Professor Antoni Zygmund, and "Finite Deformations of an Elastic Solid," by Professor F. D. Murnaghan. There were six sections for contributed papers, one of which was a joint session with the Institute of Mathematical Statistics. Eighty-eight papers were presented either in person or by title.

THE National Research Council announces that fellowships in mathematics, astronomy, physics, chemistry, geology, paleontology, physical geography, zoology, botany, agriculture, forestry, anthropology and psychology will be available for the year 1944–1945. These fellowships are awarded as a rule to persons under thirty-five years of age who are citizens of the United States or Canada, and who have met all the requirements for the doctor's degree. Applications must be filed on or before December 31, on forms obtainable from the secretary of the Fellowship Board in the Natural Sciences, National Research Council, 2101 Constitution Avenue, Washington 25, D. C. A handbook describing the fellowships—stipends, conditions and tenure—will be furnished upon request.

SCIENCE SERVICE announces that the membership in Science Clubs of America has increased 300 per cent. since this time last year. The third annual science talent search, sponsored by Science Clubs of America and offering $11,000 in Westinghouse science scholarships, is now under way. Entries must be completed by December 27. Over 15,000 high-school seniors competed in a similar contest last year, and it is expected that more than that number will enter this third search for talented science students worthy of financial assistance for higher education.

THE State Legislature of Alabama has made an appropriation making possible the inauguration of a state-wide program of cancer control. For the first year $30,000 has been set aside and for the second year $50,000 to finance the project, which will be administered by the State Board of Health. A cancer control committee has been named by the Medical Association of the State of Alabama.

DISCUSSION

A POSSIBLE RELATIONSHIP BETWEEN THE WALNUT ERINOSE MITE AND WALNUT BLIGHT

IN the late summer of 1942, successful isolation of the walnut blight organism, *Phytomonas juglandis* (Pierce) Bergey *et al.*, responsible for huge annual losses of English walnuts all over the world, was made from a walnut erinose mite, *Eriophyes tristriatus* Nalepa var. *erinea* Nalepa, found hibernating beneath the scales of a healthy, dormant bud on an English walnut tree. Transferred to the surface of a plate of beef agar, colonies of bacteria in mixed culture, including the blight organism, developed from one of a small number of mites so treated. After purification of the cultures, needle puncture inoculations were made on the main stems of young seedling walnuts forced in the greenhouse. Small but characteristic lesions of the disease developed before the trees went dormant and the tissue hardened.

In 1943, young shoots and nuts on mature trees inoculated by the needle puncture method likewise developed characteristic lesions. Similarly, broth suspensions of the bacteria atomized on unwounded nuts produced numerous lesions. Corresponding controls in all the experiments referred to remained healthy.

Smith[1] pointed out over thirty years ago that flies attracted to the black, slimy sap that often oozes from blight lesions and which teems with the bacteria may become contaminated. Since wounds or abrasions of the epidermis of susceptible tissue are not necessary for infection, he assumed that flies disseminate the disease by simply tracking the bacteria over susceptible surfaces, or on their mouth parts. It must be recognized that flies are not obligate parasites[2] of the walnut and their presence in a tree is casual or accidental. Thus the role they play in the dissemination of the disease must be a variable one if they actually constitute a factor at all.

The successful isolation of the blight bacteria from the walnut erinose mite marks the first instance that a strictly obligate parasite of the English walnut has been found to harbor the organism. Whether the walnut erinose mite can actually transmit the disease to the nuts is not yet proved, but it does not seem im-

[1] C. O. Smith, *Calif. Agr. Exp. Sta. Bul.* 231, 1912.

[2] Even the walnut husk fly, a serious parasite of walnuts in Southern California, is not an obligate parasite of the walnut. The first authentic report of its presence in the state occurred as late as 1926, consequently the flies C. O. Smith worked with were entirely different and probably not parasites on walnuts at all.

probable. The mites, microscopic in size, are omnipresent on walnuts and abound by the millions on trees of all sizes and ages where they produce erinea or galls on the foliage. Heretofore, except for the hypertrophies they produce on the leaves, they have been regarded as of no importance. In the light of the present discovery it may be necessary to take them more seriously. This is true with regard to existing methods of controlling bacterial blight, since the sprays now in use for controlling the disease do not destroy the mite. This factor may be responsible for certain irregularities observed from time to time in the control of the disease with sprays.

Grateful acknowledgment is made to Dr. Leslie M. Smith, one of the few authorities on Eriophyid mites in California, for his considerable assistance in handling the mites used in the experiments.

B. A. RUDOLPH

DECIDUOUS FRUIT STATION,
UNIVERSITY OF CALIFORNIA,
SAN JOSE, CALIF.

ANOTHER DISCOVERY OF CHAOS CHAOS

IN 1936 Schaeffer[1] rediscovered Chaos Chaos in a New Jersey marsh. In the spring of 1942, we found several large specimens of the animal in a shallow pond in Cunningham Park, New York City. In the spring of 1943, we collected several large specimens, some measuring 900 μ, in the same pond.

These animals responded readily to culturing by the method of Brandwein.[2] The agar which serves to anchor the rice grains (as described in this method) was eliminated. Large quantities of these animals are now on hand. They are able to ingest such animals as Frontonia, Stentor, Spirostomum, Blepharisma, different Rotifera and some of the smaller Turbellaria.

The animals seem to be Schaeffer's type A, in the main. Some of the animals, however, have the ellipsoid nucleus of the so-called type B.

PAUL F. BRANDWEIN
PATRICIA PENN
CLARE SHIEL

FOREST HILLS HIGH SCHOOL,
FOREST HILLS, N. Y.

TENNYSON'S PREDICTION OF THE INVENTION, USE AND MISUSE OF THE AEROPLANE

ON several previous occasions I have, in these columns, drawn attention to a number of remarkable predictions concerning the invention, use and misuse of aeroplanes. In all these cases the prophets were scientists. I have elsewhere drawn attention to similar predictions made by literary men.[1] The prediction concerning the aeroplane which is perhaps the most remarkable of all is by Alfred Tennyson, and occurs in his poem "Locksley Hall," published in 1842.[2]

The relevant stanzas are as follows:

Men, my brothers, men the workers, ever reaping something new:
That which they have done but earnest of the things that they shall do;

For I dipt into the future, far as the human eye could see,
Saw the Vision of the world, and all the wonders that would be;

Saw the heavens fill with commerce, argosies of magic sails,
Pilots of the purple twilight, dropping down with costly bales;

Heard the heavens filled with shouting, and there rained a ghastly dew
From the nation's airy navies grappling in the central blue;

Far along the world-wide whisper of the south-wind rushing warm,
With the standards of the people plunging thro' the thunder-storm;

Till the war-drum throbb'd no longer, and the battle-flags were furl'd
In the Parliament of man, the Federation of the world.

There the common sense of most shall hold a fretful realm in awe,
And the kindly earth shall slumber, lapt in universal law.

So I triumph'd, ere my passion sweeping thro' me left me dry,
Left me with the palsied heart, and left me with the jaundiced eye;

Eye, to which all order festers, all things here are out of joint,
Science moves, but slowly, slowly, creeping on from point to point:

Slowly comes a hungry people, as a lion creeping nigher,
Glares at one who nods and winks behind a slowly-dying fire:

Yet I doubt not thro' the ages one increasing purpose runs,
And the thoughts of men are widen'd with the process of the suns.

M. F. ASHLEY MONTAGU

HAHNEMANN MEDICAL COLLEGE
AND HOSPITAL,
PHILADELPHIA

[1] A. A. Schaeffer, *Turtox News*, 15: 114–115, 1937.
[2] P. F. Brandwein, *American Naturalist*, 69: 628, 1935.

[1] "Four on War," *Technology Review*, April, 1943.
[2] *Poems by Alfred Tennyson*, 2 vols., London, 1842.

SCIENTIFIC BOOKS

HEAT ENGINES

The Theory and Practice of Heat Engines. By D. A. WRANGHAM. xii + 756 pp. Illustrated. Cambridge at the University Press. $10.50.

IN setting out to place under one cover all the details about heat engines from history to the latest gas turbine work, the author has indeed chosen a Herculean task. Is it any wonder then that the reader on closing the book is left with a confused opinion of good, bad, indifferent? In the preface appears the sentence, "In writing this book the author has kept in mind the tremendous amount of ground which the student of to-day is expected to cover." Who expects the student to cover so much? This expectation is a debatable one pedagogically; and the resulting textbook—it is certainly not a treatise—is a debatable one from many points of view.

Again in the preface, "In the treatment of this subject the author has endeavored to reduce things to their first elements, . . . ," a noble goal indeed. But there follows, "For this reason the molecular theory has been introduced . . ." as though this were the basis of the operation of heat engines. The real basic theory of the interrelation of thermal energy to mechanical energy is the branch of science known as thermodynamics. The beauty and generality of thermodynamics lies in the fact that all the results follow from a few simple laws entirely devoid of any assumptions about the microscopic constitution of matter. Thermodynamics in heat engines as in other applications is not a sterile theory but supplies the basic formulas by which all energy computations are made. Kinetic theory on the other hand may supply to the study of heat engines an intellectually pleasing and sometimes useful qualitative picture of events, but it does not supply any useful quantitative results which can not better be obtained from thermodynamics. The author is entirely correct when he says, "There is very little to be remembered in the fundamental laws which control heat engines, but it is in their application where troubles arise," but it is disappointing to find nowhere in the book a clear statement of what these fundamental laws are. The student new to the subject must indeed be clever to find the unstated fundamental laws in operation in the "large number of worked examples . . . included . . . for this reason."

This picture of the unsatisfactory treatment of the *theory* of heat engines would not be complete without the quotation of a few of the many statements which are sufficiently vague to defy classification or which put in the same sentence unrelated material. On page 8, "In England practical engineers are brought up on the Fahrenheit scale, and can think only in terms of it. Now since these men have but few computations to make. . . ." This is an argument for the use of the Centigrade scale. On page 14, "Such a volume of gas (358 cu. ft. at N.T.P.) is known as a Mol and is a more convenient unit than a cubic foot; the misfortune is that such a quantity was not introduced before the foot, otherwise we might have had a better system of units." On page 51, "A gas is said to expand adiabatically if no caloric heat is extracted from or rejected to an *External Source,* and that internally there is neither chemical action nor other losses which would reduce the stock of internal energy." Is this statement consistent with the first law of thermodynamics? And now from later in the book, page 377, in a section on "Value of Dimensionless Ratios" there appears the following: "Further, a curve which is to represent the complete relation between the quantities involved should have the same dimensions for ordinate as for abscissae, so that the function is virtually plotted against itself." An interesting nontechnical point appears on p. 504. In discussing chemical symbols ". . . only the first letter of the English or Latin names of the commoner elements is used to denote it; whilst less common elements, . . . are distinguished by an additional letter, thus: Carbon is denoted by C, Chlorine is denoted by Cl" and Argon by A and Silver by Ag, etc.

Many of the doubtful statements in the book are to long or too technical to quote in this review, but the essence of the criticism is that the fundamental laws of nature governing heat engines are not made sufficiently clear, either by statement or in application, to even be discovered by any one but an informed reader.

So far this review has had few nice things to say about the book. To stop at this point would be unfair. The author is certainly well informed on the details of construction and operation of many types of heat engines. These include modern power plant equipment as well as those of historical importance. The brief historical sketch at the beginning of each new type of equipment was both interesting and informative.

The very generous number of examples worked in minute detail is certainly admirable. In many places the examples seem to be too difficult for the text preceding them, but otherwise are well chosen to illustrate the kinds of problems encountered in practice.

The book attempts to cover the thermodynamic, fluid flow, and heat transfer aspects of all types of heat engines and their auxiliary equipment. There is treated in order heat power cycles, air compressors

and motors, reciprocating steam engines, refrigeration, condensers, steam turbines, power plants, internal combustion engines and steam boilers. While many constructional details are given, no discussion of the mechanical problems to be met in their design is attempted. However, under each type of equipment an enumerated list of advantages and disadvantages is given which helps the reader to form a balanced opinion on current models of heat engines.

The book contains a very generous number of figures and illustrations, many of which are printed in color. These add much to the clarity of the material presented as well as to amusement. Fig. 17 for example shows a Carnot cycle complete with source, the sun with a face, and a sink, icebergs, polar bear and all. In the preface the author notes that text-books like any given item of engineering practice have an average life of only ten years. This book serves to bring similar earlier texts up to date, a purpose that is accomplished, but nothing more.

HOWARD W. EMMONS

HARVARD UNIVERSITY

SPECIAL ARTICLES

THE IN-VITRO DESTRUCTION OF CAROTENE BY WATER EXTRACTS OF MINCED RAT STOMACHS IN THE PRESENCE OF METHYL LINOLATE

SHERMAN[1] has demonstrated that carotene administered to vitamin A deficient rats is inactivated by the simultaneous feeding of methyl linolate. The destructive action of the methyl linolate can be prevented by small amounts of α-tocopherol. It was shown that the carotene was destroyed in the gastrointestinal tract, but the exact site and the mechanism of the destructive action was not clear. The mixing of the carotene and methyl linolate with the basal ration, *in vitro*, did not elucidate the problem, since in this case carotene destruction occurred much too slowly to explain the *in vivo* results. The same was true when the carotene and linolate were mixed with stomach or intestinal contents. Results similar to the above have been noted by Quackenbush, Cox and Steenbock[2] and by Hickman, Harris and Woodside.[3]

This paper offers a possible explanation of the above results by demonstrating the rapid *in vitro* destruction of carotene by a clear water-extract of minced rat stomach in the presence of methyl linolate.

The stomach extract is prepared by suspending the minced stomach mucosa of the freshly killed rat in ten times its weight of distilled water, allowing it to stand for 15 minutes and then centrifuging at high speed for 10 minutes. The supernatant liquid has a dry matter content of 5 mg per ml. The extract must be clear. If the minced stomach is ground in a mortar before extracting it is impossible to clarify by centrifuging and such extracts show no carotene destructive potency when tested according to the method described below.

For purposes of comparison the mode of action and potency of the so-called "carotene oxidase" or lipoxidase[4] of the soybean has been investigated. A 0.5 per cent. suspension of the ground soybean was centrifuged after standing for 30 minutes. This extract contained 2 mg of dry matter per ml.

The carotene-destroying potency of the above extracts is determined as follows. One ml. of a 0.25 per cent. solution of highly purified methyl linolate in acetone is placed in a 125 ml Erlenmeyer flask. Ten ml of water is added, followed by one ml of McIlvaine's citric acid-sodium phosphate buffer, pH 5.7, and one ml of carotene in acetone (equivalent to 68 micrograms of carotene). Finally the extract to be tested is added (usually one ml), the flask stoppered and incubated for periods up to 30 minutes at 38° C. The reaction is stopped with hydrochloric acid and the carotene is transferred to 50 ml of ethyl ether by vigorous shaking until the water phase is clear and colorless. The carotene is then determined colorimetrically by means of the Evelyn photoelectric colorimeter. For the control, a flask containing the linolate, carotene, water and buffer is incubated as above; hydrochloric acid is added and followed by the extract under test. The carotene is immediately extracted with ether. The recovery of carotene in this case is always above 95 per cent. of the amount added. The carotene destructive potency of the material under test is calculated as the percentage loss with reference to the control run at the same time.

The results of the destructive action on carotene of increments of stomach extracts of normal adult rats are shown in Table 1. The potency of the extract is greatly reduced by heating on a boiling water water bath for 15 minutes. Without methyl linolate the action of the stomach extract is insignificant.

The action of the stomach extract is very similar to that of soybean "carotene oxidase." However, some differences do exist which indicate that the active agent is not the same in both cases. From Table 2 it is evident that although the soybean enzyme is inhibited

[1] W. C. Sherman, *Proc. Soc. Exp. Biol. and Med.*, 47: 199, 1941; *Jour. Nutrition*, 22: 153, 1941.

[2] F. W. Quackenbush, R. P. Cox and H. Steenbock, *Jour. Biol. Chem.*, 145: 169, 1942.

[3] K. C. D. Hickman, P. L. Harris and M. R. Woodside, *Nature*, 150: 91, 1942.

[4] R. J. Sumner, *Jour. Biol. Chem.*, 146: 215, 1942.

TABLE 1

THE DESTRUCTION OF CAROTENE BY WATER EXTRACTS OF MINCED RAT STOMACH MUCOSA AS COMPARED WITH SOYBEAN "CAROTENE OXIDASE"

Volume extract	Rat stomach mucosa extract*			Sobyean extract		
	Number of determinations	Destruction of carotene		Number of determinations	Destruction of carotene	
		Range	Average		Range	Average
ml		*Per cent.*	*Per cent.*		*Per cent.*	*Per cent.*
1.0	6	57.8–86.2	74.2	6	70.0–78.5	74.0
0.5	6	61.0–79.7	70.8	4	48.8–72.8	61.9
0.25	2	58.8–69.1	64.0	..	.....	...
0.20	4	51.0–55.8	54.1	2	40.0–44.4	42.2
0.10	1	.....	45.3	2	28.7–32.5	30.6
0.05	1	.....	28.0	..	.....	...
1.0 (no Linolate)	5	0–28.0	12.2	3	0–35.0	15.0
1.0 (heated)†	1	.....	36.8	..	.....	...
0.5 "	1	.....	32.8	..	.....	...
0.1 "	1	.....	20.0	..	.....	...

* Rats were on a stock diet: Average weight of the six rats used was 215 grams.
† The extract was heated on a boiling water bath for 15 minutes.

by a water extract of a low-grade wheat flour, the active agent in the stomach extract is not. On the other hand, the stomach extract appears to be more susceptible to inhibition by α-tocopherol than does the soybean extract. A further point of difference between the two extracts became evident in a study of the pH activity curves. Over a pH range of 3.0 to 6.6 using the citric acid-sodium phosphate buffer system the soybean lipoxidase was inactive below pH 4.0 and showed its maximum at about pH 5.5; the falling off was gradual on the alkaline side of the optimum. However, the rat stomach showed considerable activity even at pH 3.0. This may have a relation to a natural resistance to the acidity of the normal stomach possessed by this active carotene-destroying agent. In other respects the pH activity curve of the stomach extract was very similar to that of the soybean enzyme. The pH optimum was 5.7 and the falling off on the alkaline side was gradual.

TABLE 2

COMPARATIVE INHIBITION OF RAT STOMACH AND SOYBEAN "CAROTENE OXIDASE" BY TOCOPHEROL AND CENTRIFUGED 5 PER CENT. WATER EXTRACT OF SECOND CLEAR WHEAT FLOUR

Incubation time	Rat stomach extracts* †			Soybean extracts†		
	Number of determinations	Destruction of carotene		Number of determinations	Destruction of carotene	
		Range	Average		Range	Average
Minutes		*Per cent.*	*Per cent.*		*Per cent.*	*Per cent.*
15	5	35.5–65.9	52.6	3	65.1–70.5	67.6
30	14	56.8–81.9	70.1	3	71.3–80.8	76.0
30 (plus flour extract)	5	51.5–78.9	66.8	5	23.6–43.5	37.1
15 (1 mg) (Tocopherol)	1	.....	5.0	1	.....	42.0
30 (1 mg) (Tocopherol)	1	.....	25.0	1	.....	45.5

* Rats had been on a synthetic ration composed of 30 per cent. lard, 5.5 per cent. salts, 25 per cent. casein, sucrose and synthetic vitamins. Average weight was 178 grams.
† One ml of extracts used.

Other organs have been tested for a carotene-destroying agent in their water extracts. Preliminary results have shown that liver is quite potent while muscle and small intestine appear to have little or no potency. However, it should be mentioned that the extracts of small intestines were not clear and contained a large amount of extraneous material. As mentioned above, lack of clarity in stomach extracts indicates a resistance to destruction of carotene, and the same may be the case with the intestinal extracts. The fact that muscle extract shows no potency appears to exclude the possibility that the destructive action of the tissue extracts on carotene is an artifact resulting from iron-porphyrins or similar compounds extracted from the blood contained within the organs.[5]

Some time after the above results were obtained an attempt was made to repeat certain phases but with slightly anomalous results. No apparent change in the procedure was made, but a new supply of methyl linolate was employed, with the result that a lag phase of from one to two hours incubation time was noted during which little or no destruction of carotene occurred. However, after this time interval carotene destruction began and proceeded rapidly to near completion within 30 minutes. The general results were the same as previously noted, in that methyl linolate was required in conjunction with the stomach extract, neither being effective by itself. This peculiarity may have been caused by a small amount of an antioxidant in the new batch of linolate, or it may have been related to a variation in the efficiency of extraction of the active agent from the minced stomach.

E. L. HOVE

LABORATORY OF ANIMAL NUTRITION,
ALABAMA POLYTECHNIC INSTITUTE

AN UNIDENTIFIED NUTRIENT REQUIRED FOR PROPER UTILIZATION OF DL-ALPHA-TOCOPHEROL BY THE CHICK[1]

DURING attempts to study the rôle of vitamin E in chick nutrition with a simplified ration, the chick was not protected from a vitamin E and A deficiency when

[5] F. Haurowitz, P. Schwerin and M. M. Yenson, *Jour. Biol. Chem.*, 140: 353, 1941.

[1] Technical Contribution No. 107, South Carolina Agricultural Experiment Station. Published by permission of the director of the South Carolina Agricultural Experiment Station. We are indebted to Merck and Company, Inc., Rahway, N. J., for dl-alpha-tocopherol; Anheuser-Busch and Company, St. Louis, Mo., for dried brewers' yeast; Distillation Products, Inc., Rochester, N. Y., for vitamin A; Central Soya Company, Inc., Decatur, Indiana, for soybean phosphatides; and E. I. du Pont de Nemours and Company, New Brunswick, N. J., for vitamin D_3.

these vitamins were included in the ration at a level several times the requirement. Slanetz and Scharf[2] reported that soybean phosphatides promoted proper utilization of vitamin A in the rat. Quackenbush, Cox and Steenbock[3] found that dl-alpha-tocopherol was an antioxidant for vitamin A and carotene.

The percentage composition of the basal ration was as follows: Dextrin 52.3, Cellophane 3, casein (purified) 30, gelatin 5, salts 4.6, lard 5 and choline 0.1. In addition each one hundred grams of the ration contained 200 I. U. vitamin D_3, 800 I. U. vitamin A (natural esters), 0.1 mg 2-methyl-1,4-naphthoquinone, 0.5 mg thiamin, 1 mg riboflavin, 0.5 mg pyridoxin, 2 mg Ca-pantothenate, 2 mg nicotinic acid, 30 mcg biotin, 1 mg inositol and a fuller's earth eluate equivalent to 12 grams of dried brewers' yeast. This ration is adequate in all water-soluble nutrients required for normal growth of the chick; however, it is inadequate in vitamin E and an unrecognized fat-soluble substance which is necessary for proper utilization of vitamin E. This unrecognized nutrient is found in yeast and soybean phosphatides. It can be removed from yeast by extraction with hot Skellysolve B and is soluble in ether, Skellysolve B and Stoddard solvent.

The data presented in Table 1 summarize the study on the unrecognized fat-soluble nutrient. Chicks receiving only the basal ration (Trial 1) started to develop vitamin E deficiency symptoms at about 12 days of age, and by the 28th day severe vitamin A and E deficiency symptoms were present. Those receiving 0.001 per cent. dl-alpha-tocopherol, trial 2, developed vitamin A and E deficiency symptoms simultaneously with those in trial 1. When the basal ration was supplemented with 0.001 per cent. dl-alpha-tocopherol plus 5 or 10 per cent. dried brewers' yeast, they developed normally. If they received 0.001 per cent.

TABLE 1

INFLUENCE OF DIFFERENT SUPPLEMENTS ON THE DEVELOPMENT OF VITAMIN E AND A DEFICIENCY SYMPTOMS IN CHICKS

Trial	Supplement to basal ration	Observations up to 5 weeks of age: Mortality	Vitamin E deficiency	Vitamin A deficiency
		Per cent.	Per cent.	Per cent.
1	None	100	83	100
2*	dl-alpha-Tocopherol	100	90	100
3*	dl-alpha-Tocoperol, 5 per per cent. yeast	0	0	0
4*	dl-alpha-Tocopherol, 10 per cent. yeast	0	0	0
5*	dl-alpha-Tocopherol, 2 per cent. soybean phosphatides	0	0	0
6*	dl-alpha-Tocopherol, 5 per cent. extracted yeast	100	70	100
7	5 per cent. extracted yeast	100	60	100
8*	dl-alpha-Tocopherol, massive vitamin A dosage.	20	67	0

* dl-alpha-Tocopherol was added at a level of 0.001 per cent.

dl-alpha-tocopherol plus 5 per cent. brewers' yeast which had been extracted for 72 hours in a Soxhlet extractor with hot Skellysolve B, they developed vitamin E and A deficiency symptoms. If the basal ration was made adequate in dl-alpha-tocopherol and supplemented with 2 per cent. soybean phosphatides the chick developed normally. When the chicks were given massive dosages of vitamin A (4,000 I. U. per day) for the first three days of life and also the basal ration made adequate in vitamin E, they developed only vitamin E deficiency during the first 35 days of life.

H. PATRICK
C. L. MORGAN

POULTRY DEPARTMENT,
CLEMSON AGRICULTURAL COLLEGE,
SOUTH CAROLINA

SCIENTIFIC APPARATUS AND LABORATORY METHODS

A METHOD FOR INDICATING THE MOISTURE CONTENT OF FOODS DURING DEHYDRATION[1]

IN the dehydration of foods, such as vegetables, fruits, meats, etc., there is a great need for a method which will indicate, in the dehydrators, the moisture content of the dehydrating material and which will tell when the material has dried to the proper or preferred moisture content and is ready to be removed. At the present time, three different methods are used for this purpose: (1) appearance and feel of the material by hand; (2) taking a sample and determining its moisture content; and (3) dehydrating the material for a definite and predetermined length of time. Obviously, for one reason or another, these methods can not be considered entirely satisfactory.

It is the purpose of this note to present a method which can be used in dehydrators to indicate, by proper calibration, the moisture content of the dehydrating material at the various stages of dehydration and to tell when the material has dried to the proper or preferred moisture content and is ready to be removed.

The method is based upon the well-known phenomenon that the evaporation of water lowers the temperature. When the fresh material is being dehydrated, there are two temperatures, that of the chamber and that of the material itself. At the beginning, when

[2] C. A. Slanetz and A. Scharf, *Proc. Soc. Exp. Biol. and Med.*, 53: 17, 1943.

[3] F. W. Quackenbush, R. P. Cox and H. Steenbock, *Jour. Biol. Chem.*, 145: 169, 1942.

[1] Journal article No. 660, new series.

the material contains its maximum water content, the evaporation of the water lowers its temperature far below that of the chamber. As the material becomes progressively drier its temperature becomes progressively higher, until finally both temperatures come close together. At this point, the material reaches a degree of dryness which is very close to the commonly desired moisture content.

The procedure consists of placing two thermometers in the dehydrator. The bulb of one thermometer is bare and is simply hanging in the chamber. The bulb of the second thermometer is covered with a definite amount of the dehydrating material contained in a small bag of cheesecloth and is placed on one of the loaded trays. The bag with the material is held around the bulb by rubber bands which tend to exert pressure continuously. The area and amount of material placed in the cheesecloth bag are definite and constant and are related to the amount and thickness of the layer of the material on the trays.

The cheesecloth bag technique is universal in application, in that, by means of it, almost any kind of material can be tied around the bulb of the thermometer. For example, peas and carrots can be tied as effectively and readily as slices of potatoes, apples or leaves of spinach.

The thermometers used in this method are specially devised and are well suitable for the purpose. They are electrical resistance thermometers, using, as resistor, a liquid instead of metal. They have a range from 2,500,000 ohms at 32° F. to 25,000 at 185° F. They are about 30,000 times more sensitive than the metallic electrical resistance thermometers. The electrical resistance values are read on a special wheatstone bridge. The bulb of the thermometers is made of glass and is 25 mm long and 8 mm in diameter. The wire leads are composed of the ordinary lamp-cord and can be of any length. These new electrical thermometers seem to be admirably suited for dehydration work. The wire leads make it possible and convenient to read the temperatures from the outside of the dehydrator.

The type of results obtained by this method is shown in Fig. 1. The material dehydrated is cabbage. It will be seen that the electrical resistance of the uncovered thermometer attains the temperature of the chamber very quickly and fluctuates as that temperature varies. The electrical resistance of the covered thermometer, however, remains at a higher level (lower temperature) for some time, and when the bulk of the water is evaporated, it begins to decrease, and finally almost reaches, to within 1,000 ohms, the resistance of the uncovered thermometer. At this point, the moisture content of the cabbage is 4.5 per cent., by vacuum oven determination, which is close to the lower range of the preferred moisture content. It is clearly evident from this chart that by calibration it is possible to know during the dehydration when the material has reached the desired moisture content.

The method has been tested on almost all the various materials commonly dehydrated, and in every case it has proven successful, dependable and accurate. Relying entirely upon this method, it has been possible to dehydrate many materials for the first time down to the preferred moisture content with surprisingly persistent accuracy and without resorting to any other aid. Results of checks agreed to within about 1 per cent.

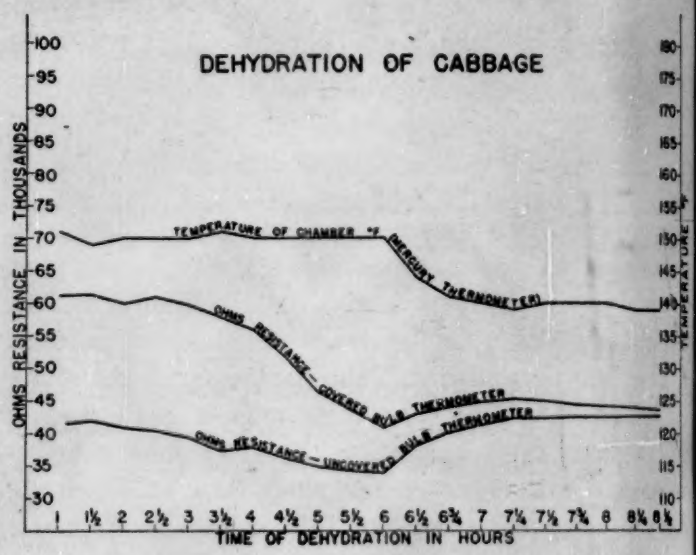
DEHYDRATION OF CABBAGE
OHMS RESISTANCE IN THOUSANDS
TEMPERATURE
TEMPERATURE OF CHAMBER °F. (MERCURY THERMOMETER)
OHMS RESISTANCE — COVERED BULB THERMOMETER
OHMS RESISTANCE — UNCOVERED BULB THERMOMETER
TIME OF DEHYDRATION IN HOURS

FIG. 1

While the method has been used thus far mainly in the non-moving type of dehydrators, there is no reason why it can not be adopted and used also in the conveyor or any other type of dehydrator.

The method is based upon sound fundamental principles and should fill the great need for a simple, direct and reliable method for indicating the moisture content of the dehydrating material, and for telling when the material has reached the desired moisture content and is ready to be taken out of the dehydrators. A comprehensive report is forthcoming.

GEORGE BOUYOUCOS
H. A. CARDINELL

MICHIGAN AGRICULTURAL EXPERIMENT STATION,
EAST LANSING

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